









[*From the Journal of Physiology.* Vol. V. No. 1.]

[1887]



PHYSIOLOGICAL ACTION OF CONDURANGO. By T.  
LAUDER BRUNTON, M.D, F.R.S., *Assistant Physician and  
Lecturer on Materia Medica at St. Bartholomew's Hospital.*

ALL the experiments which I have performed for the purpose of ascertaining the physiological action of Condurango were made with a watery extract prepared for me by Mr Jeffs, Dispenser to St. Bartholomew's Hospital<sup>1</sup>.

*Characters of the Extract of Condurango.*

One ounce of the extract was obtained from one pound of the root. It was of a dark brown, almost black colour, slightly aromatic odour and a bitter taste. It was very soluble in water and formed a dark brown opaque solution.

*General Action of the Extract on Frogs.*

Some of the experiments here detailed were made with the double purpose of ascertaining the influence of Condurango on reflex action as well as its general action, and the animals were therefore in these experiments suspended, instead of being allowed to move freely on a level surface.

EXPERIMENT I. Five grains of the extract of Condurango were suspended in six minims of water and  $\frac{7}{8}$ ths of the mixture ( $4\frac{3}{8}$  grains) injected under the skin of the back of a large frog, tolerably strong but not so active as most of the others. It was then covered by a glass jar. The frog remained quiet when left to itself but moved actively when touched. No effect seemed to be produced by the Condurango for an hour afterwards.

Twenty-four hours after the frog was again examined and seemed totally unaffected. Four days afterwards it was found to be somewhat languid, and five days after the injection it was dead.

<sup>1</sup> The experiments recorded in this paper were all made in the autumn of 1871.

EXPERIMENT II. A strong frog was suspended by the fore legs and two grains of solid extract were introduced under the skin of the abdomen. Immediately afterwards the frog seemed somewhat more restless than before, and drew up its legs more quickly when they were touched. Its movements were performed in the same way after the injection as before it. When placed on a level surface it seemed quite unaffected by the Condurango, and continued to be so for the next ten days during which it was observed.

EXPERIMENT III. One grain of extract mixed with a few drops of water was injected under the skin of the back of a strong frog suspended in the same way as the other. Immediately afterwards it became restless, and seemed also uneasy when touched. Otherwise it remained unaffected, and no effect of the Condurango could be observed during the next ten days.

EXPERIMENT IV. Two grains of the extract mixed with a few drops of water were injected under the skin of the back of a frog suspended like the others. The result was the same as in Experiment III.

EXPERIMENT V. Five grains of the extract were suspended in water and injected under the skin of the back of a strong frog. The frog was suspended by the head. It seemed somewhat restless after the injection but no other effect could be observed. Next day it seemed in its normal condition and on the third day also.

EXPERIMENT VI. The same experiment as in V. was repeated with a like result.

EXPERIMENT VII. The same as in V. and VI. No result was observed at first. Next day the frog seemed weak, and when laid on its back could not turn over so readily as the others. It was a smaller frog than the others. On the third day it seemed well.

These experiments show that the extract of Condurango when injected under the skin of frogs produces no effect even when such a large dose as 5 grains is administered.

The restlessness which is noted in those hung up was in all probability due to the injection of the fluid, and not to the action of the drug, as it occurred immediately after the operation and before there had been time for much to be absorbed.

The death of one frog after the injection can hardly be attributed to the Condurango, as the animal was observed to be less active than the others previous to the injection, and death did not occur till several days afterwards.

*General Action on Mammals.*

The experiments on this point were made exclusively on Rabbits.

EXPERIMENT VIII. One gramme (15·4 grains) of the extract was dissolved in 20 cub. cent. of a solution of one part NaCl in 200 of water. It was dissolved in  $\frac{1}{2}$  per cent. NaCl solution in preference to water in order to avoid the irritation which water itself produces when brought in contact with the tissues of the body. Ten cubic centimetres of this solution were injected into the peritoneal cavity of the body weighing 936 grammes (2 lb. 1 oz.).

No effect whatever was observed.

34 minutes afterwards the remaining 10 cub. cent. were injected. No effect was produced. The solution had not been filtered.

In order to test the effect of the injection of saline solution itself, 10 cub. cent. were injected into the peritoneal cavity of a rabbit weighing 425 grammes (1 lb. 15 oz.).

It produced no effect.

Next day both animals were perfectly well and lively. They seemed to have passed a good deal of water during the night, but as they were both in the same cage it was impossible to say how much had been passed by each. Both animals were kept under observation for several days but no further effect of the injection was noticed. The increased urination was probably only due to the water which had been injected.

EXPERIMENT IX. One gramme (15·4 grs.) of extract was mixed with 10 cub. cent. of water. The solution was not filtered and contained little particles. A cannula was placed in the jugular vein of a rabbit weighing 1030 grammes (2 lb. 4 oz.) and  $1\frac{1}{4}$  cubic centimetres of the solution were injected into it. No apparent effect was produced.

15 minutes afterwards one cub. cent. more was injected; three minutes after the second injection the respiration was much quicker, and five minutes afterwards one cub. cent. more was injected.

One minute after the last injection the animal's hind legs spread out laterally, and it sank down on its fore paws.

In  $\frac{1}{2}$  minute more it turned on its side: its head became drawn backwards on its shoulders so as to form almost a right angle with the body, and it gave one or two convulsive kicks. Its eyes then became very prominent and the cornea insensible to the touch.

*Post-mortem Examination.* The body was immediately opened. When the abdominal muscles were divided the legs gave a twitch. The heart was still found pulsating, though only feebly. The right cavities were full, but the left cavities were empty.

In this experiment the injection of about one-third of a gramme (5 grs.) of the extract into the jugular vein was followed by death, whereas in Experiment VIII. the injection of three times this dose into the peritoneal cavity of a smaller rabbit produced no effect. As drugs are generally absorbed with great rapidity from the peritoneal cavity the difference between the results of the two experiments could hardly be due to non-absorption of the Condurango in Experiment VIII. and it was therefore in all probability due to something not connected with the action of the drug.

The hurried breathing, convulsions and death which followed the injection of the unfiltered solution of the extract into the jugular vein, as well as the distension of the cavities on the right side of the heart and the emptiness of those on its left, seemed to indicate that the death of the rabbit in Experiment IX. was due to the production of emboli in the pulmonary artery by the undissolved particles of extract.

In order to test this conclusion the following experiment was made.

EXPERIMENT X. One gramme (15.4 grs.) of the extract was dissolved in 20 cub. cent. of warm water and filtered. When first thrown on the filter it passed rapidly through, but in the course of a minute or two it began to pass through very slowly. As soon as it began to do this the fluid was emptied out of the first filter and thrown upon a fresh one. In this way the filtrate was obtained quickly but might contain very fine particles which had passed through the filter and might have been removed by it afterwards.

A cannula was placed in the jugular vein of a rabbit weighing 680 grammes ( $1\frac{1}{2}$  lb.) and 10 cub. cent. of the filtrate were slowly injected into it. During the injection the respiration became hurried and occasionally a convulsive twitch of the limbs occurred. A few minutes afterwards five cub. cent. more were injected. The animal was then released. It tumbled much and seemed weak but could move about perfectly well. Its respiration was laboured. Twenty hours afterwards it seemed weak and languid and its respiration somewhat hurried.

In this experiment nearly  $\frac{3}{4}$  of a gramme were injected into the jugular vein of a rabbit weighing 680 grammes with the effect of producing hurried respiration and weakness. In Experiment IX. the injection of  $\frac{1}{3}$  of a gramme was followed by the death of a rabbit weighing 1030 grammes.

The difference between these experiments consisted in the solution of Condurango being filtered in Experiment X. and *not* in Experiment

IX. and we must therefore conclude that the fatal result in the latter case was due to the presence of large particles in the fluid.

The hurried breathing in Experiment X. might be due to the small particles which had passed through the filter but were yet large enough to become impacted in the pulmonary capillaries.

*Results of Experiments on the General Action of the Extract of Condurango.*

Condurango has no poisonous action.

The extract produced no apparent effect on frogs when given in doses of  $\frac{1}{3}$  of a gramme (5 grs.), or on a rabbit in a dose of 1 gramme ( $15\frac{1}{2}$  grs.), an amount which is equivalent to 72 grammes ( $2\frac{1}{2}$  oz.) of the extract, or  $2\frac{1}{2}$  lb. of the root for a man weighing 150 lb. The convulsions which occurred in Experiment IX. were in all probability due to embolism of the pulmonary artery and not to the action of the Condurango. The statement of Gianuzzi and Bufalini<sup>1</sup> that Condurango has a convulsant action like strychnia probably depends on a mistaken misinterpretation of the results of experiments like that of Experiment IX. although I cannot be certain on this point, as I have never been able to see their original paper.

It has no paralysing action, and apparently no action of any kind on voluntary muscles or motor nerves, as the movements of the animals were unaffected by its administration.

*Effect of Condurango on Reflex Action.*

As Condurango produces no *apparent* effect, and as Dr. Joseph Xavier Eguigusen states that "it cannot be administered many days in succession because in some persons nervous phenomena of importance supervene", it seemed possible that its action might resemble that of quinine.

The following experiments were therefore undertaken in order to ascertain whether it had, like quinine, the power of diminishing reflex action.

They were performed in the usual way, by suspending a frog by the fore-arms or head and noting by the aid of a metronome the time which elapsed before it drew its foot out of a very dilute mixture of sulphuric acid and water. Extract of Condurango was then injected under

<sup>1</sup> *Ricerche eseguite nel Gabinetto di Fisiologia della Universita di Siena*, pp. 71—86, abstracted in the *Centralblatt d. med. Wissenschaften*, 1873, p. 824.

the skin, the foot again dipped in dilute acid, and the time till it was pulled out compared with that which had been noted before the injection.

To show that the mere suspension of the frog and the successive irritations applied to the feet had no effect on the time required for reflex action, a frog into which nothing was injected was suspended at the same time as the others.

EXPERIMENT XI. Four frogs were suspended by their arms, and their feet irritated by very dilute sulphuric acid. After each application of the acid the foot was carefully washed.

In the following account *R* stands for right foot, *L* for left foot, and the numbers under each indicate the number of seconds before the foot was drawn out of the dilute sulphuric acid.

| Time.                | Frog I. |     | Frog II. |     | Frog III. |     | Frog IV. |     | Remarks.                                                                                                                                                         |
|----------------------|---------|-----|----------|-----|-----------|-----|----------|-----|------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                      | R.      | L.  | R.       | L.  | R.        | L.  | R.       | L.  |                                                                                                                                                                  |
|                      |         |     |          |     |           |     |          |     | Frog I. was tested first, but on dipping its right foot into the acid, it became apparent that it was too strong. It was therefore diluted and again applied.    |
| 3 <sup>h</sup> . 20' |         | 12" | 5"       | 15" | 7"        | 6"  | 5"       | 5"  |                                                                                                                                                                  |
| " 35'                | 12"     | 10" | 12"      | 12" | 12"       | 16" | 6"       | 6"  |                                                                                                                                                                  |
| " 38'                | 12"     | 10" | 13"      | 6"  | 13"       | 20" | 4"       | 8"  |                                                                                                                                                                  |
| " 45'                | 13"     | 13" | 12"      | 13" | 13"       | 17" | 6"       | 10" |                                                                                                                                                                  |
|                      | 15"     | 25" | 11"      | 12" | 20"       | 20" | 8"       | 10" |                                                                                                                                                                  |
| 4 <sup>h</sup> . 0'  |         |     |          |     |           |     |          |     | Two grains of extract of Condurango were suspended in a few drops of $\frac{3}{4}$ per cent. Nu Cl solution, and injected under the skin of the back of Frog IV. |
| " 3'                 |         |     |          |     |           |     | uneasy   |     |                                                                                                                                                                  |
| " 5'                 |         |     |          |     |           |     | quiet    |     |                                                                                                                                                                  |
| " 10'                | quiet   |     | uneasy   |     | quiet     |     |          |     |                                                                                                                                                                  |
| " 12                 |         |     |          |     | uneasy    |     | uneasy   |     | On touching the feet of Frogs II. III. and IV., they drew them away much more readily than Frog I.                                                               |
|                      | 26"     | 28" | 12"      | 30" | 18"       | 46" | 4"       | 8"  | Reflex action again tested by acid.                                                                                                                              |
|                      | 32"     | 40" | 10"      | 12" | 18"       | 25" | 6"       | 8"  |                                                                                                                                                                  |
|                      | 46"     | 34" | 8"       | 8"  | 11"       | 22" | 9"       | 7"  |                                                                                                                                                                  |

Frog I. was not so lively as the others, and it will be seen from the next Experiments that the diminution of reflex action which occurred in it during this experiment is not a general rule but is due to an individual peculiarity.

EXPERIMENT XII. Two frogs were suspended by the head and reflex action tested by dilute sulphuric acid (one part acid to 250 of water).

During the experiment both frogs struggled a good deal, and when a severe struggle occurred just before the acid was applied to the foot reflex action seemed to be somewhat diminished.

| Time.                          | Frog I. |     | Frog II. |     | Remarks.                                                                                                    |
|--------------------------------|---------|-----|----------|-----|-------------------------------------------------------------------------------------------------------------|
|                                | R.      | L.  | R.       | L.  |                                                                                                             |
| 1 <sup>h</sup> . 33'           | 10"     | 49" | 26"      | 42" | Acid of 1 in 300 was here used.<br>Frog I. struggled much after acid had been applied to the right foot.    |
|                                | 8"      | 14" | 10"      | 11" | Acid of 1 in 250 here used.                                                                                 |
|                                | 13"     | 14" | 11"      | 11" |                                                                                                             |
|                                | 14"     | 14" | 4"       | 7"  |                                                                                                             |
| 2 <sup>h</sup> . 57'           |         |     |          |     | Five grains of extract of Condurango suspended in water was injected under the skin of the back of Frog II. |
| abt. 3 <sup>h</sup> .          | 9"      | 11" | 54"      | 26" |                                                                                                             |
| 5 <sup>h</sup> . 53'           | 10"     | 8"  | 17"      | 30" |                                                                                                             |
| Twenty hours }<br>afterwards } | 4"      | 10" | 36"      | 62" |                                                                                                             |
|                                | 20"     | 16" | 41"      | 35" |                                                                                                             |
|                                | 12"     | ?   | 15"      | 20" | Frog II. very restless.                                                                                     |

During the night they were taken down and had rested.

EXPERIMENT XIII. Two frogs suspended, and reflex action tested with sulphuric acid (1 to 250 water).

| Time.                          | Frog I. |    | Frog II.       |     | Remarks.                                                                                                                        |
|--------------------------------|---------|----|----------------|-----|---------------------------------------------------------------------------------------------------------------------------------|
|                                | R.      | L. | R.             | L.  |                                                                                                                                 |
|                                | 1"      | 3" | 4"             | 6"  |                                                                                                                                 |
|                                | 2"      | 3" | 2"             | 5"  |                                                                                                                                 |
|                                | 2"      | 1" | 5"             | 6"  |                                                                                                                                 |
| 2 <sup>h</sup> . 58'           |         |    |                |     | Five grains of the extract of Condurango suspended in a few drops of water were injected under the skin of the back of Frog II. |
|                                |         |    | Frog<br>uneasy |     |                                                                                                                                 |
| abt. 3 <sup>h</sup> . 5'       | 2"      | 3" | 8"             | 10" | Frog I. remained untouched.                                                                                                     |
| 5 <sup>h</sup> . 58'           | 1"      | 1" | 5"             | 6"  |                                                                                                                                 |
| Twenty hours }<br>afterwards } | 4"      | 2" | 5"             | 7"  | They were taken down at night and not left suspended.                                                                           |
|                                | 2"      | 4" | 11"            | 12" |                                                                                                                                 |

EXPERIMENT XIV. Two frogs were suspended by the head, and reflex action tested by applying dilute sulphuric acid (1 part acid in 250 of water) to the feet.

| Time.                          | Frog I. |     | Frog II. |     | Remarks.                                                                                                                   |
|--------------------------------|---------|-----|----------|-----|----------------------------------------------------------------------------------------------------------------------------|
|                                | R.      | L.  | R.       | L.  |                                                                                                                            |
| 2 <sup>h</sup> . 26'           | 11"     | 8"  | 8"       | 5"  |                                                                                                                            |
| „ 32'                          | 9"      | 8"  | 11"      | 7"  |                                                                                                                            |
| „ 52'                          | 10"     | 6"  | 6"       | 4"  |                                                                                                                            |
| „ 59'                          |         |     |          |     | Five grains extract of Condurango, suspended in a few drops of water, were injected under the skin of the back of Frog II. |
|                                |         |     |          |     | Frog I. was untouched.                                                                                                     |
| 3 <sup>h</sup> . 10'           | 12"     | 10" | 9"       | 8"  | Frog II. became uneasy and restless immediately after the injection.                                                       |
| abt. 6 <sup>h</sup> .          |         |     | 8"       | 10" | Frog I. had escaped and could not be found.                                                                                |
| Twenty hours }<br>afterwards } |         |     | 11"      | 17" |                                                                                                                            |
|                                |         |     | 12"      | 18" |                                                                                                                            |

For greater convenience in comparing the results of these experiments I subjoin the mean number of seconds required for reflex action in each of the frogs during the time they were suspended before Condurango was injected into some of them, and the number of seconds required during the time they hung after the injection had been made.

EXPERIMENT XI.

|                              | Frog I.                          |      | Frog II.                       |                                | Frog III.                      |                                | Frog IV.                       |                                |
|------------------------------|----------------------------------|------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|
|                              | Uninjured.                       |      | had 2½ grs. extract.           |                                | had 2 grs. extract.            |                                | had 2 grs. extract.            |                                |
|                              | R.                               | L.   | R.                             | L.                             | R.                             | L.                             | R.                             | L.                             |
| In the time before injection | 12 <sup>3</sup> / <sub>4</sub>   | 14   | 10 <sup>3</sup> / <sub>5</sub> | 11 <sup>3</sup> / <sub>5</sub> | 13                             | 15 <sup>4</sup> / <sub>5</sub> | 5 <sup>4</sup> / <sub>5</sub>  | 7 <sup>4</sup> / <sub>5</sub>  |
| After                        | 34 <sup>2</sup> / <sub>3</sub>   | 34   | 10                             | 16 <sup>2</sup> / <sub>3</sub> | 15 <sup>2</sup> / <sub>3</sub> | 31                             | 6 <sup>1</sup> / <sub>3</sub>  | 7 <sup>2</sup> / <sub>3</sub>  |
| Difference                   | 21 <sup>11</sup> / <sub>12</sub> | 20   | 3 <sup>3</sup> / <sub>5</sub>  | 5 <sup>1</sup> / <sub>15</sub> | 2 <sup>2</sup> / <sub>3</sub>  | 15 <sup>1</sup> / <sub>5</sub> | 8 <sup>8</sup> / <sub>15</sub> | 2 <sup>2</sup> / <sub>15</sub> |
|                              | more                             | more | less                           | more                           | more                           | less                           | more                           | less                           |

## EXPERIMENT XII.

|                              | Frog I.                 |                        | Frog II.                |                         |
|------------------------------|-------------------------|------------------------|-------------------------|-------------------------|
|                              | Uninjured.              |                        | 5 grs.<br>extract.      |                         |
|                              | R.                      | L.                     | R.                      | L.                      |
| In the time before injection | $11\frac{2}{3}$         | 14                     | $8\frac{1}{3}$          | $9\frac{2}{3}$          |
| After                        | $10\frac{3}{4}$         | $11\frac{1}{4}$        | $32\frac{3}{5}$         | 39                      |
| Difference                   | $\frac{11}{12}$<br>less | $2\frac{3}{4}$<br>less | $24\frac{4}{5}$<br>more | $29\frac{1}{3}$<br>more |

## EXPERIMENT XIII.

|                              | Frog I.                |                        | Frog II.                      |                         |
|------------------------------|------------------------|------------------------|-------------------------------|-------------------------|
|                              | Uninjured.             |                        | Got 5 grs. of<br>the extract. |                         |
|                              | R.                     | L.                     | R.                            | L.                      |
| In the time before injection | $1\frac{2}{3}$         | $2\frac{1}{2}$         | $3\frac{2}{3}$                | $5\frac{2}{3}$          |
| After                        | $2\frac{1}{4}$         | $2\frac{3}{4}$         | $7\frac{1}{2}$                | $8\frac{3}{4}$          |
| Difference                   | $\frac{7}{12}$<br>more | $\frac{5}{12}$<br>more | $3\frac{7}{12}$<br>more       | $3\frac{1}{12}$<br>more |

## EXPERIMENT XIV.

|                              | Frog I.    |    | Frog II.                  |                         |
|------------------------------|------------|----|---------------------------|-------------------------|
|                              | Uninjured. |    | Got 5 grs.<br>of extract. |                         |
|                              | R.         | L. | R.                        | L.                      |
| In the time before injection | 10         | 8  | $8\frac{1}{3}$            | $5\frac{1}{3}$          |
|                              |            |    | 10                        | $10\frac{3}{4}$         |
|                              |            |    | $1\frac{2}{3}$<br>more    | $5\frac{5}{12}$<br>more |

Difference between the number of seconds required for reflex action during the time the frogs were suspended before the injection of Condurango, and in the time after the injection.

## Uninjured Frogs.

|                   | R.                          | L.      |
|-------------------|-----------------------------|---------|
| Frog I. Expt. XI. | $21\frac{11}{12}$ more      | 20 more |
|                   | In the time after injection |         |

|                    |                      |                     |
|--------------------|----------------------|---------------------|
| Frog I. Expt. XII. | $\frac{11}{12}$ less | $2\frac{3}{4}$ less |
| " " XIII.          | $\frac{7}{12}$ more  | $\frac{5}{12}$ more |

## Frogs which received Condurango.

| R.                    | L.                   |          |           |        |               |
|-----------------------|----------------------|----------|-----------|--------|---------------|
| $\frac{3}{5}$ less    | $5\frac{1}{15}$ more | Frog II. | Expt. XI. | 2 grs. | solid extract |
| $2\frac{2}{3}$ more   | $15\frac{1}{5}$ more | „ III.   | „ „       | 2 grs. | in water      |
| $\frac{3}{15}$ more   | $\frac{2}{15}$ less  | „ IV.    | „ „       | 2 grs. | „             |
| $24\frac{4}{15}$ more | $29\frac{1}{3}$ more | „ II.    | „ XII.    | 5 grs. | „             |
| $3\frac{7}{12}$ more  | $3\frac{1}{12}$ more | „ II.    | „ XIII.   | 5 grs. | „             |
| $1\frac{2}{3}$ more   | $5\frac{5}{12}$ more | „ II.    | „ XIV.    | 5 grs. | „             |

In only one of these experiments (Experiment XII.) does any marked diminution of reflex excitability occur after the injection of Condurango. Nearly as great a diminution is to be observed in Experiment XI. Frog I. where nothing had been injected, and it is therefore probable that the exceptional diminution in Experiment XII. as well as in Experiment XI. Frog I. is to be ascribed to an individual peculiarity of the frog and not to the action of the Condurango.

In most of the other experiments we find a slight diminution of reflex excitability, but it is very slight and might be due to the exhaustion produced by the struggles of the animal after the injection of the drug.

*Conclusions regarding the Effect of Condurango on Reflex Action.*

Unlike quinine Condurango has very little effect on reflex action. A slight diminution of reflex excitability was observed after the injection of the extract into frogs in doses of 2 or 5 grains, but the number of experiments is insufficient to show whether or not this was due to the exhaustion produced by the struggles of the frog.

*Effect of Condurango on Circulation and Respiration.*

EXPERIMENT XV. A cannula was placed in the trachea of a rabbit and connected by india-rubber tubing with a T tube, to one limb of which was attached a stopcock which allowed of more or less free communication with the atmosphere and the other limb of which was in connection with one of Marey's cardiographic levers which registered the respirations on a revolving cylinder. By increasing or diminishing the resistance which the stopcock opposed to the entrance of air into the tracheal cannula the amplitude of the excursions of the lever could be altered at will.

The blood-pressure was registered by a kymographion connected with a cannula in the left carotid of the rabbit. The number of cardiac pulsations was estimated from the undulations produced by them in the blood-pressure tracings.

| Time.                     | Blood-pressure.            | Pulse.              | Respirations.       | Remarks.                                                                                                                                                                                                                                                                                                                                                                                                     |
|---------------------------|----------------------------|---------------------|---------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                           | in millimetres of Mercury. | in $7\frac{1}{2}$ " | in $7\frac{1}{2}$ " |                                                                                                                                                                                                                                                                                                                                                                                                              |
| abt. 4 <sup>h</sup> . 15' | 120                        | 21                  | $6\frac{3}{4}$      | Each 6 <sup>th</sup> respiration became larger than the others when the injection was made.                                                                                                                                                                                                                                                                                                                  |
|                           | 120                        | 18                  | $6\frac{1}{2}$      | 5 cub. cent. of a suspension of 4 grammes extract in water was injected into the peritoneal cavity.                                                                                                                                                                                                                                                                                                          |
|                           |                            |                     |                     | The respirations became deeper and the undulation in the tracing of the blood pressure corresponding to every 6 <sup>th</sup> respiration becomes very distinct, while previously it was very slight.                                                                                                                                                                                                        |
| abt. 4 <sup>h</sup> . 23' | 120                        | 17                  | 6                   | This seems due to the pain of the injection and the excitement of the animal after it.                                                                                                                                                                                                                                                                                                                       |
|                           |                            |                     |                     | Injected about $2\frac{1}{2}$ cub. cent. more. The undulations in the pressure curve again became more distinct and the respirations much more forced.                                                                                                                                                                                                                                                       |
| 4 <sup>h</sup> . 32'      | 114                        | 20                  | $6\frac{1}{2}$      |                                                                                                                                                                                                                                                                                                                                                                                                              |
| 5 <sup>h</sup> . —        | 108                        | ?                   | 7                   |                                                                                                                                                                                                                                                                                                                                                                                                              |
|                           |                            |                     |                     | Attempted to inject more solution into the peritoneum, but the tube seemed stopped up and the solution would not enter. A clot now formed in the cannula in the carotid, so it was cleaned out. In order to prevent the blood from passing too far into it after readjustment, the bicarbonate solution of soda was passed into it at a pressure nearly equal to that at which the blood had formerly stood. |
|                           |                            |                     |                     | When the artery was again connected with the manometer it was found that the blood pressure had fallen, and therefore some of the bicarbonate of soda in all probability passed into the artery.                                                                                                                                                                                                             |
| 5 <sup>h</sup> . 21'      | 86                         |                     |                     |                                                                                                                                                                                                                                                                                                                                                                                                              |
|                           | 70                         | 16                  | 8                   |                                                                                                                                                                                                                                                                                                                                                                                                              |
|                           | 66                         |                     |                     |                                                                                                                                                                                                                                                                                                                                                                                                              |
| 5 <sup>h</sup> . 21'.45"  |                            |                     |                     | Injected 4 cub. cent. of a saturated solution of extract of Condurango in $\frac{3}{4}$ per cent. solution which had been filtered while hot into the jugular vein.                                                                                                                                                                                                                                          |

| Time.                    | Blood-pressure.            | Pulse.              | Respirations.       | Remarks.                  |
|--------------------------|----------------------------|---------------------|---------------------|---------------------------|
|                          | in millimetres of Mercury. | in $7\frac{1}{2}$ " | in $7\frac{1}{2}$ " |                           |
| 5 <sup>h</sup> . 22'     | 60                         | 14                  | $8\frac{1}{2}$      | Cardiac pulsation larger. |
| 5 <sup>h</sup> . 22'.15" | 50                         | $12\frac{1}{2}$     | 8                   |                           |
| 5 <sup>h</sup> . 22'.30" | 56                         | 13                  | 8                   |                           |
| 5 <sup>h</sup> . 23'     | 64                         |                     | 8                   |                           |
| 5 <sup>h</sup> . 24'.30" | 64                         | 14                  |                     |                           |
| 5 <sup>h</sup> . 30'     | 48                         | $15\frac{1}{2}$     | 9                   |                           |

The animal was then killed.

EXPERIMENT XVI. A cannula was placed in the trachea of a rabbit and connected as in the previous experiment with one of Marey's levers by a T tube and a stopcock.

The movements of the registering lever were increased or diminished according to the greater or less resistance which the stopcock opposed to the entrance of air into the T tube.

A second cannula was placed in the left carotid and connected with a kymographion which registered the blood-pressure. The number of cardiac pulsations was ascertained by counting the undulations which they produced in the blood-pressure.

The Condurango was injected through a cannula in the jugular vein.

### Tracing I.

|                    | Time.            | Blood-pressure.            | Pulse.              | Respirations.       | Remarks.                                                                                                                                                                                                        |
|--------------------|------------------|----------------------------|---------------------|---------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                    |                  | in millimetres of Mercury. | in $7\frac{1}{2}$ " | in $7\frac{1}{2}$ " |                                                                                                                                                                                                                 |
|                    |                  | 102                        | 35                  | $7\frac{1}{2}$      |                                                                                                                                                                                                                 |
| After irritation } | $7\frac{1}{2}'$  | 46                         | 7 ?                 | 15 ?                | Right vagus irritated by an interrupted current. Respiration trembling and imperfect. Irritation stopped after continuing for $7\frac{1}{2}$ ". The pulse immediately became quick and the blood-pressure rose. |
|                    | 15'              | 122                        |                     | $11\frac{1}{2} ?$   |                                                                                                                                                                                                                 |
|                    | $22\frac{1}{2}'$ | 107                        |                     | $12 ?$              |                                                                                                                                                                                                                 |
|                    | 30'              | 106                        | 30                  | $14\frac{1}{2}$     |                                                                                                                                                                                                                 |
|                    | $37\frac{1}{2}'$ | 98                         | 36                  | $11\frac{1}{2}$     |                                                                                                                                                                                                                 |

*Tracing II.*

|                                            | Time.            | Blood-<br>pressure.                | Pulse.              | Respi-<br>rations.  | Remarks.                                                                                                                        |
|--------------------------------------------|------------------|------------------------------------|---------------------|---------------------|---------------------------------------------------------------------------------------------------------------------------------|
|                                            |                  | in milli-<br>metres of<br>Mercury. | in $7\frac{1}{2}$ " | in $7\frac{1}{2}$ " |                                                                                                                                 |
| Some<br>minutes<br>after Trac-<br>ing I. } |                  | 104                                |                     | $9\frac{1}{2}$      | 5 cub. cent. of a cold<br>saturated solution of Con-<br>durango were filtered and<br>injected into the right ju-<br>gular vein. |
| after injection                            | $10\frac{1}{2}'$ | 96                                 | 34                  | $9\frac{1}{2}$      |                                                                                                                                 |
|                                            |                  | 96                                 | 33                  | $9\frac{1}{2}$      |                                                                                                                                 |

*Tracing III.*

|                  |                                    |     |                 |                 |                                                           |
|------------------|------------------------------------|-----|-----------------|-----------------|-----------------------------------------------------------|
|                  | after begin-<br>ning of<br>Tracing | 87  |                 |                 |                                                           |
|                  | 15'                                | 83  | 33              | 10              |                                                           |
|                  | $22\frac{1}{2}'$                   | 74  |                 | 10              |                                                           |
|                  | 30'                                | 77  | 30              | 10              |                                                           |
|                  | $37\frac{1}{2}'$                   | 75  |                 | $9\frac{1}{2}$  |                                                           |
|                  | 45'                                | 75  | 30              | $9\frac{1}{2}$  |                                                           |
|                  | $52\frac{1}{2}'$                   | 78  |                 | 10              |                                                           |
|                  | 60'                                | 75  |                 | 10              |                                                           |
| 1 <sup>h</sup> . | $7\frac{1}{2}'$                    | 75  |                 | $9\frac{1}{2}$  |                                                           |
|                  | 15'                                | 75  |                 | 9               | Right vagus irritated.<br>— The nerve was not<br>divided. |
|                  | $22\frac{1}{2}'$                   | 63  |                 |                 |                                                           |
|                  | 30'                                | 73  | 14              | 5               |                                                           |
|                  | $37\frac{1}{2}'$                   | 83  | $12\frac{1}{2}$ | 7?              | Irritation continuing.                                    |
|                  | 45'                                | 88  | 13              | 12?             |                                                           |
|                  | $52\frac{1}{2}'$                   | 93  | 13              | 15              |                                                           |
| 2 <sup>h</sup> . |                                    | 95  | 13              | 14              | Irritation stopped.                                       |
|                  | $7\frac{1}{2}'$                    | 122 | 30              | $13\frac{1}{2}$ |                                                           |
|                  | 15'                                | 124 | 28              | 11              |                                                           |
|                  | $22\frac{1}{2}'$                   | 113 |                 | 11              |                                                           |
|                  | 30'                                | 106 | 30              | $11\frac{1}{2}$ |                                                           |
|                  | $37\frac{1}{2}'$                   | 101 |                 | $10\frac{1}{2}$ |                                                           |
|                  | 45'                                | 99  |                 | 11              |                                                           |
|                  | $52\frac{1}{2}'$                   | 98  |                 | $11\frac{1}{2}$ |                                                           |

*Tracing IV.*

|  |                  |     |                 |  |                                                                                                   |
|--|------------------|-----|-----------------|--|---------------------------------------------------------------------------------------------------|
|  |                  | 93  |                 |  |                                                                                                   |
|  | $7\frac{1}{2}'$  | 94  |                 |  |                                                                                                   |
|  | 15'              | 102 | 12              |  | Right vagus irritated.<br>Irritation continuing.<br>Respiration very weak.<br>Irritation stopped. |
|  | $22\frac{1}{2}'$ | 102 | $10\frac{1}{2}$ |  |                                                                                                   |
|  | 30'              | 102 | $10\frac{1}{2}$ |  |                                                                                                   |
|  |                  |     |                 |  |                                                                                                   |

Tracing V.

|  | Time.                | Blood-pressure.            | Pulse. | Respirations. | Remarks.                                                                                                                                                                                                |
|--|----------------------|----------------------------|--------|---------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  |                      | in millimetres of Mercury. | in 7½" | in 7½"        |                                                                                                                                                                                                         |
|  | 7½'                  | 99                         |        |               | Both vagi divided.<br>The pressure curve shows large undulations which do not correspond with the respiratory or pulse wave, but extend over a period nearly equal to that occupied by 2½ respirations. |
|  | 15'                  | 103                        |        | 5             |                                                                                                                                                                                                         |
|  | 22½'                 | 102                        |        | 4             |                                                                                                                                                                                                         |
|  | 30½'                 | 101                        |        | 4             |                                                                                                                                                                                                         |
|  | 37½'                 | 100                        | 34 ?   | 5             |                                                                                                                                                                                                         |
|  | 45'                  | 95                         |        | 4½            | Peripheral extremity of the right vagus irritated.<br>Irritation stopped.                                                                                                                               |
|  | 52½'                 | 94                         | 11     | 4½            |                                                                                                                                                                                                         |
|  | 1 <sup>h</sup> .     | 98                         |        | 5             |                                                                                                                                                                                                         |
|  | 1 <sup>h</sup> . 7½' | 94                         |        | 4½            |                                                                                                                                                                                                         |

The animal was now killed.

EXPERIMENT XVII.

A strong rabbit weighing 6 lbs. was experimented on. The respirations, pulse, and blood-pressure were recorded as in the previous experiments.

|            | Time. | Blood-pressure.            | Pulse. | Respirations. | Remarks.       |
|------------|-------|----------------------------|--------|---------------|----------------|
|            |       | in millimetres of Mercury. | in 7½" | in 7½"        |                |
| Tracing I. | 7½'   | 131                        |        |               | Both vagi cut. |
|            | 15'   | 131                        | 30     | 8             |                |
|            | 22½'  | 131                        | 30     | 8½            |                |
| II.        | 7½'   | 128                        | 34     | 6             |                |
|            | 15'   | 129                        | 34     | 5             |                |
|            | 30'   | 128                        | 33     | 5             |                |
|            | 37½'  | 128                        | 33     | 5             |                |
|            | 45'   | 126                        |        | 5½            |                |
|            | 52½'  | 127                        | 34½    | 5½            |                |
|            |       |                            |        |               |                |

## Tracing III.

|             | Time.              | Blood-pressure.            | Pulse. | Respirations. | Remarks.                                                                                        |
|-------------|--------------------|----------------------------|--------|---------------|-------------------------------------------------------------------------------------------------|
|             |                    | in millimetres of Mercury. | in 7½" | in 7½"        |                                                                                                 |
|             | 1 <sup>h</sup> .   | 129                        |        | 5½            |                                                                                                 |
|             | 7½'                | 128                        |        | 5½            |                                                                                                 |
|             | 15'                | 127                        | 33     | 4½            |                                                                                                 |
|             | 15½'               |                            |        |               | Vagus irritated and heart stopped.                                                              |
|             |                    |                            |        |               | Blood pressure fell during the first stoppage 38 mm. in $\frac{8}{34}$ of a second.             |
|             | 18½'               | 46                         |        |               |                                                                                                 |
|             | 22½'               | 150                        |        |               | The electrodes were then less closely applied to the nerve, and the pressure rose.              |
|             | 30'                | 142                        | 34½    | 6             |                                                                                                 |
|             |                    |                            |        |               | After the irritation ceased three respirations succeeding it were much smaller than the others. |
|             | 33'                |                            |        |               | Vagus again irritated. The blood-pressure sank 48 mm. in $\frac{9}{34}$ of a second.            |
|             | 37½'               | 47                         | 2?     | 7             | } Irritation stopped.                                                                           |
|             | 39½'               | 36                         | 0      |               |                                                                                                 |
|             | 43½'               |                            | 0      | 7½            |                                                                                                 |
|             | 45'                | 92                         |        |               |                                                                                                 |
|             | 47'                | 186                        |        |               | Respiration very small.                                                                         |
|             | 52½'               | 162                        |        | 6             |                                                                                                 |
|             | 2 <sup>h</sup> . 0 | 160                        | 32½    | 5½            |                                                                                                 |
|             | 7½'                | 126                        |        |               |                                                                                                 |
|             | 15'                | 123                        | 36     | 6             |                                                                                                 |
| Tracing IV. |                    |                            |        |               |                                                                                                 |
|             | 7½'                | 123                        |        |               |                                                                                                 |
|             | 15'                | 122                        | 35     | 5½            |                                                                                                 |
|             | 22½'               | 124                        |        | 5½            |                                                                                                 |
|             | 30'                | 120                        | 27     | 5½            |                                                                                                 |

|                   | Time.                 | Blood-pressure.            | Pulse. | Respirations. | Remarks. |
|-------------------|-----------------------|----------------------------|--------|---------------|----------|
|                   |                       | in millimetres of Mercury. | in 7½" | in 7½"        |          |
| <i>Tracing V.</i> | 7½'                   | 120                        | 28     | 6             |          |
|                   | 11'                   |                            |        |               |          |
|                   | 15'                   | 122                        | 31     | 7             |          |
|                   | 22½'                  | 127                        |        | 6             |          |
|                   | 30'                   | 125                        | 31     | 5½            |          |
|                   | 37½'                  | 123                        | 32     | 5½            |          |
|                   | 45'                   | 123                        |        | 6             |          |
|                   | 52½'                  | 123                        | 32½    | 6             |          |
|                   | 55'                   |                            |        |               |          |
|                   | 1 <sup>h</sup> .      | 123                        | 33½    | 5½            |          |
|                   | 7½'                   | 122                        |        | 6             |          |
|                   | 15'                   | 119                        | 32     | 5½            |          |
|                   | 16½'                  |                            |        |               |          |
|                   | 21'                   | 61                         |        |               |          |
|                   | 1 <sup>h</sup> . 22½' | 99                         |        |               |          |
|                   | 27'                   | 106                        | 8½     | 6             |          |
|                   | 30'                   | 136                        |        |               |          |
|                   | 37½'                  | 118                        |        | 5½            |          |

Began to inject a solution of Condurango (filtered) into the jugular vein. Injected 10 c. c. containing 25 grammes of extract.

Injection finished.

Left vagus irritated. Blood-pressure fell 38 mm. in  $\frac{6}{34}$ ths of a second.

Irritation stopped.

At this time peculiar curves began to appear in the blood-pressure tracing. I could not understand in the very least what their cause was at the time, but when the experiment was finished I found that a clot of blood had formed in the tracheal cannula, which would obstruct the breathing, and was in all probability the occasion of these curves. As this would complicate to a great extent the effects observed I have not noted this part of the experiment.

*Results of Experiments XV. XVI. and XVII.*

|             | Blood-pressure | Pulse.              | Respiration.        | Remarks.                                             |
|-------------|----------------|---------------------|---------------------|------------------------------------------------------|
| Expt. XV.   | unaltered      | slightly slower     | slightly slower     | Injection of 1 gramme of extract into the peritoneum |
|             | somewhat less  | quickened to normal | quickened to normal | ½ gramme more.                                       |
|             | less           | slower              | no effect           | Injection into the jugular.                          |
| Expt. XVI.  | less           | no effect           | quicker             | do. do.                                              |
| Expt. XVII. | unaltered      | quicker             | quicker             | ¼ gramme into jugular ;—vagi cut.                    |

These experiments show that Condurango has no action on the pressure of the blood when it is injected into the peritoneum in large doses. The diminished blood-pressure noticed in some instances might be due to the animal's strength being diminished by its position on the board and the effects of the operations. Its effect on the pulse and respiration is not constant, the injection being sometimes followed by quickening and sometimes by slowing, and moreover the results which followed its injection into the jugular might in some degree be due to the presence of fine particles in it having a mechanical effect.

The whole subject of the pulmonary circulation, the action of drugs upon it and the effect which changes in it produces upon other parts of the body, is at present very imperfectly known, and it is therefore extremely difficult or impossible to say what the effect of such fine particles as were contained in the solution of extract might be when they once enter the pulmonary vessels.

For the purpose of ascertaining whether Condurango had any effect in contracting or dilating the arterioles and capillaries, the vagus was irritated so as to stop the heart, and the rapidity with which the blood-pressure fell during the stoppage of the heart before the injection was compared with that which was found after it.

#### EXPERIMENT XVII. *Tracing II.*

|                                                              |                                                       |
|--------------------------------------------------------------|-------------------------------------------------------|
| Blood-pressure fell 38 mm. in $\frac{8}{34}$ ths of a second | } <i>before</i> injection<br>of $\frac{1}{4}$ gramme. |
| " " 48 " $\frac{9}{34}$ " "                                  |                                                       |
| " " 24 " $\frac{5}{34}$ in one pulse wave                    |                                                       |
| " " 38 " $\frac{6}{34}$ ths of a second                      | } <i>after.</i>                                       |
| " " 18 " $\frac{5}{34}$ in one pulse wave                    |                                                       |

These numbers show that with the instrument employed no definite conclusion can be drawn regarding the state of contraction of the arterioles, but indicate that no extensive alteration was produced in them by the Condurango.

It may seem strange that I have not made any experiments on the effect of Condurango on tissue change as indicated by the amount of urea and salts in the urine more especially, as it has been recommended especially in cases where a drug possessing an influence over tissue change would be likely to be serviceable. The experiments of Boeck have however shown that those drugs, such as iodine, morphine and quinine, which have some effect upon tissue change produce but very

slight alterations compared with those which result from variations in food, and Toldt and Nowak have found that the amount of Nitrogen varies even in the flesh of the same animal, so that it would be almost necessary to analyze the flesh eaten every day as well as rigorously to fix its amount, and this would be more than anyone could well undertake who could not devote his whole time to the work.

### *General Summary.*

Watery extract of Condurango has no action on frogs even when injected into the dorsal lymph-sac in doses of 5 grains. On rabbits it has no poisonous action when injected into the peritoneal cavity. When a solution containing fine particles in suspension is injected into the jugular vein the animal dies with symptoms of opisthotonos. When the coarser particles are removed this does not occur although the breathing is quickened. It is not improbable that the quickening of the breathing is due to the lodgments of fine particles in the pulmonary capillaries and that the opisthotonos which I noticed in one experiment (Exp. IX.) and which has been supposed by Granuzzi and Bufalini to be due to the direct action of Condurango on the nerve centres was really due to asphyxia caused by pulmonary embolism.

Unlike quinine Condurango has very little effect on reflex action<sup>1</sup>.

Condurango when injected into the peritoneum even in large doses has no action on the blood-pressure.

It does not exert any definite action on the arterioles nor does it paralyze the peripheral terminations of the vagus.

<sup>1</sup> Since the preceding experiments were made Mr Pardington and I have found that the diminution in reflex excitability which Chaperon described as caused by the injection of quinine into the lymph-sac of the frog probably depends on the local irritation produced by the acid in which the quinine is dissolved.





